CLAIMS

1. A multiply reflecting time-of-flight mass spectrometer (MR TOF MS) comprising:
a pulsed ion source;
an ion receiver;
a set of two parallel gridless ion mirrors, substantially elongated in shift direction; A drift space between the said mirrors;
the above elements being arranged to provide a folded ion path between the ion source and the receiver, composed of multiple reflections between the ion mirrors and of a displacement in the shift direction;
the said MR-TOF MS separating ions in time according to their mass to charge ratio so that the flight time is substantially independent of ion energy;
wherein for the purposes of improving resolution and sensitivity a set of 2 or more lenses is positioned in the said drift space along said shift direction, with a period in the shift direction corresponding to ion shift per integer number of ion reflections.
2. The MR-TOF MS of claim 1, wherein each of the said ion mirrors comprises at least 4 electrodes to provide independence of time-of-flight of ions on initial spatial spread across the plane of the folded ion path.
3. The MR-TOF MS of claim 1, wherein said pulsed ion source comprises an ion source of the following list: SIMS, MALDI, IR MALDI, preferably incorporating any of the following devices: a) a pulsed gas supply b) an accelerator with pulsed voltages c) an accelerator with static voltages.
4. The MR-TOF MS of claim 1, wherein the said pulsed ion source comprises an ion storage device and an ion accelerator, whereas ions are produced by an intrinsically continuous ion source of the following list: ESI, APCI, APPI, EI, CI, PI, ICP, gas filled or atmospheric MALDI, gaseous ion reaction cell, DC or field asymmetric ion mobility spectrometer, or a fragmentation cell of a tandem mass spectrometer.
5. The MR-TOF MS of claim 4, wherein the said ion storage device comprises a gas-filled set of electrodes with radio-frequency (RF) voltage applied to at least one of them including any device or a combination of devices of the following list: ion guide with two or more elongated rods, 3-D quadrupole ion trap, linear ion trap with radial or axial ion ejection, RF channel with 1 or more electrodes having an opening for ion passage,

ring electrode trap, a hybrid of ion guide with a 3-D ion trap, or segmented analogs of the above devices made of flat plates.

6. The MR-TOF MS of claim 5, wherein the said ion storage device comprises two sets of electrodes, with radio-frequency voltages applied to at least one electrode of the first set and pulsed voltages applied to at least one electrode of the second set.
7. The MR-TOF MS of claim 4, wherein the said ion accelerator comprises a pulsed orthogonal accelerator, preferably made of flat electrodes with slits elongated and oriented along the shift axis of the MR-TOF MS.
8. The MR-TOF MS of claim 4, wherein the said accelerator is built into the pulsed ion mirror, or a pulsed portion of ion mirror or positioned adjacent to the ion mirror and has matching electrode shape and potentials.
9. The MR-TOF MS of claim 4, wherein the said continuous ion source comprises an additional, intermediate storage ion guide, preceding ion storage device of claim 4 and preferably having a higher gas pressure compared to the ion storage device of claim 4 and wherein said additional storage ion guide is a gas-filled set of electrodes with radio-frequency voltage applied to at least one of them including any device listed in claims 5 or 6.
10. The MR-TOF MS of claim 1, wherein for the purpose of convenient tuning the periodic lenses are substantially elongated transversely the plane of the folded ion path.
11. The MR-TOF MS of claim 1, wherein the said elongated ion mirrors are made as a parallel assembly of conductive square frames, plates with long slots, bars, rods or a like with an optional edge termination by printed circuit boards.
12. The MR-TOF MS of claim 2, wherein each of the said mirrors comprises at least two electrodes having voltages of opposite polarities relatively to each other or a potential of drift space.
13. The MR-TOF MS of claim 1, wherein at least a portion of at least one electrode of at least one ion mirror is connected to a pulsed voltage supply for ion gating in and/or out of the MR-TOF MS.
14. The MR-TOF MS of claim 1, wherein the drift space comprises means for ion deflection, connected to either a DC or pulsed voltage supplies.
15. The MR-TOF MS of claim 14, wherein the said deflection means comprises at least one set of steering plates, either planar or bent.

16. The MR-TOF MS of claim 15, wherein the steering plates have the same dimensions as electrodes of the planar lenses of claim 10 and wherein at least one steering plate is adjusted to either combine focusing and steering or to be switched between those.
17. The MR-TOF MS of claim 14, wherein at least one deflector is located on the far side of shift axis opposite to the source, such deflector steering ions in a static mode to revert the direction of ion shift.
18. The MR-TOF MS of claim 14, wherein at least one deflector is located at the source side of shift axis, such deflector is operated either to direct ions into an off axis detector, or to direct ions into the MR-TOF analyzer or in a pulsed mode to revert the direction of ion shift for the time of ion confinement within MR-TOF MS.
19. The MR-TOF MS of claim 1, wherein the ion receiver is an ion detector with an extended dynamic range including any combination of the following: a) secondary electron multiplier with at least one dynode, b) scintillator and photomultiplier, c) micro-channel or micro-sphere plates, d) two or more channels of detection, e) two or more anodes each connected to a data acquisition system, preferably including analog-to-digital converter (ADC).
20. The MR-TOF of claim 19, wherein the dynamic range of data acquisition is extended by alternating scans with various intensity of the pulsed ion source, preferably varied by adjusting a duration of ion injection into any ion storage device.
21. The MR-TOF of claims 19, wherein for the purpose of extending life time of the detector, at least one ion storage device is arranged and controlled to either filter out low mass ion components or to selectively remove or suppress the most intense ion components.
22. The MR-TOF of claim 19, wherein for the purpose of extending life time of the detector the said MR-TOF analyzer further comprises an additional timed ion selector, said selector is controlled to suppress the most intensive ionic components, determined in a preliminary scan at a lower intensity of the pulsed ion source, said selector including devices of the following list: a Bradbury-Nielsen ion gate, a parallel plate deflector, a control grid within the ion detector.
23. The MR-TOF MS of claim 1, wherein the ion receiver is a gas filled cell of the following list: a fragmenting cell, cell for ion molecular or ion-ion reactions, electron capture dissociation or a an ion capture dissociation, a cell for ion soft deposition onto a surface, a cell for surface ion dissociation, -and wherein those gaseous cells preferably have set of electrodes connected to RF voltage for ion collisional dampening and confinement.

24. A tandem multi reflecting time-of-flight mass spectrometer (MR-TOF MS-MS) comprising an MR-TOF MS of claims 1 to 23 to separate parent ions, a fragmentation cell and an additional mass spectrometer for mass analysis of fragment ions, said elements being sequentially interconnected.

25. The MR-TOF MS-MS of claim 24, wherein the fragmentation cell is filled with gas and preferably comprises an additional differential pumping stage and ion focusing means.

26. The MR-TOF MS-MS of claim 25, wherein the product of the cell length L and gas pressure P in the cell is maintained above P*L> 0.2 Torr*cm, preferably P>0.5 Torr and L< 1cm.

27. The MR-TOF MS-MS of claim 24, wherein the fragmentation cell comprises a gas filled set of electrodes with radio frequency (RF) voltage applied to at least one of them and forming any RF device of the list in claim 5 to confine ions in radial direction.

28. The MR-TOF MS-MS of claim 27, wherein the cell further comprises a set of electrodes connected to DC or slow varying voltage to form an axial DC electric field or an axial moving wave electric field, controlling velocity of ion motion in the cell, said DC voltage being applied to the same or a separate set of electrodes as RF voltage of claim 27.

29. The MR-TOF MS-MS of claim 24, wherein the said additional mass spectrometer is a time-of-flight mass spectrometer (TOF MS).

30. The MR-TOF MS-MS of claim 29, wherein the additional TOF MS comprises an orthogonal ion accelerator, preferably gridless.

31. The MR-TOF MS-MS of claim 29, wherein the second TOF MS has a shorter ion path and preferably a higher acceleration voltage, such that flight time in the said second TOF MS is at least 100-fold smaller compared to one in the MR-TOF MS and wherein the second TOF MS preferably comprises a data system for 'parallel' acquisition of fragment spectra without mixing spectra corresponding to different parent ions.

32. The MR-TOF MS-MS of claim 29, wherein the said second TOF MS is also a multi-reflecting spectrometer (MR-TOF MS) of claims 1 to 23, preferably said second MR-TOF MS is similar to the first MR-TOF MS.

33. The MR-TOF MS-MS of claim 32, wherein the second MR TOF MS comprises deflectors, preferably incorporated into some of the lenses in drift space, said deflectors are arranged to allow adjustment of flight path in the second MR-TOF.

34. The MR-TOF MS-MS of claim 32, further comprising a timed ion selector between the first MR-TOF and fragmentation cell.

35. A tandem multi reflecting time-of-flight mass spectrometer (MR TOF MS-MS) comprising an MR-TOF MS of claims 1 to 23, and a fragmentation cell, connected the said MR-TOF; wherein the said fragmentation cell comprises means for reverting ions back into the same MR-TOF for the purpose of tandem MS-MS analysis.
36. The MR-TOF MS-MS of claim 35 further comprising a set of steering plates, preferably combined with some of periodic lenses, said steering plates are arranged to allow adjustment of flight path in the said MR-TOF MS, preferably said adjustment is being different for ions coming in and out of the fragmentation cell.
37. The MR-TOF MS-MS of claim 35, wherein said means of reverting ion flow comprise electrodes and voltage sources to provide for an axial DC or a moving wave electric field.
38. A method of sample analysis using multi reflecting time-of-flight mass spectrometer, said method comprising the sequential steps of: forming ion pulses; passing ions along a multiply folded ion path, formed by reflecting ions within a two-dimensional electrostatic field and by ion displacement in a third - 'shift' - direction; receiving ions, time separated according to their mass-to-charge ratio onto an ion receiver; the said electrostatic field being formed within two planar and parallel gridless ion mirrors, separated by drift space; the said ion mirrors being tuned to simultaneously achieve a time-of-flight focusing and a spatial focusing across the plain of the folded ion path; wherein for the purposes of improving resolution, sensitivity and ease of use, the ion packets are periodically focused in the shift direction by a set of multiple periodic lenses.
39. The method of claim 38, wherein the said ion pulses are produced by an ionization method of the following list: SIMS, MALDI, IR MALDI, preferably incorporating a pulsed gas cooling, and wherein the said pulsed acceleration is delayed compared to the ionizing and cooling pulses.
40. The method of claims 38, wherein the said ion pulses are produced in the following sequence of steps: a continuous ion beam is produced by a continuous ionization method, like ESI, APCI, EI, CI, PI, ICP, SIMS or MALDI with collisional cooling; the said continuous ion beam is stored in a gas-filled volume using ion confinement by a combination of RF and DC electric fields with a subsequent pulse ejection and acceleration of ion packets.
41. The method of claim 40, wherein the said ion confinement comprises an additional preliminary step of ion storage and partial ejection of stored ion cloud, the said step

being performed in a separate compartment at a higher gas pressure, compared to the storage step preceding acceleration of ion packets.

42. The method of claims 40, wherein at least one of ion storage steps is arranged within an elongated set of electrodes with RF voltage applied to at least one of them.

43. The method of claim 40, wherein the volume occupied by ion beam during ion introduction from preliminary ion storage into the storage for pulse preparation, exceeds by at least factor of 5 the volume occupied by ion beam immediately prior to pulse ejection.

44. The method of claim 40, wherein the storage for pulse preparation is oriented along an axis, the latter being substantially parallel or orthogonal to the direction of ion acceleration towards MR-TOF, and includes radial RF field and axially trapping well, the latter formed by a combination of RF fields and constant voltages on at least some electrodes of said storage.

45. The method of claims 40, wherein at least some RF and DC voltages applied to at least some electrodes of the storage for pulse preparation are abruptly changed during or prior to the pulsed ejection of ions, preferably the RF voltage is switched off at zero phase and pulses are switched on after a predetermined time delay.

46. The method of claim 40, wherein the said pulsed ejection is achieved by a pulsed change of said DC fields within gas-filled volume without substantially changing RF field.

47. The method of claim40, wherein the said pulsed ejection is composed of two separate, frequency synchronized and time delayed steps- ejection from the gas-filled volume and a subsequent pulsed acceleration, preferably in the orthogonal direction.

48. The method of claim 38, wherein the number of ions per pulse is adjusted either at the step of ion storing, or at the step of time separation in MR-TOF MS or at the ion detection step, said adjustments being preferably made to reduce space charge effects at ion storage or to improve dynamic range and life time of the detector.

49. The method of claim 48, wherein such adjustment comprise either filtering of mass range of interest, or low mass suppression, or selective suppression of intense ion components or a non-selective adjustment of ion number per ion pulse.

50. The method of claim 48, wherein a number of ions in the second storage is alternated between scans in order to increase dynamic range of detection and data acquisition steps.

51. The method of claim 48, wherein a preliminary spectrum is acquired at least once using a substantially lower than average number of ions per cycle.

52. The method of claim 48, wherein a set of mass-to-charge ratios for ions with intensities above a certain threshold are determined, and wherein said set of mass-to-charge ratios is used to activate pulsed ion selector within MR-TOF in order to affect velocity or direction or spatial distribution of at least some portion of ions with mass-to-charge ratios from said set.

53. The method of claim 52, wherein pulsed ion selector is any of the following: Bradbury-Nielsen ion gate, parallel-plate deflector, a control grid within the ion detector.

54. The method of claim 38, wherein the said ion mirrors are arranged and tuned to provide a time of-flight focusing, substantially independent on ion width across the plane of ion path

55. The method of claim 38, wherein the said time focusing is achieved to a second order in relation to spatial, angular and energy spreads of the initial ion packet, including cross terms and wherein possible temperature and temporal drifting of such focusing is preferably compensated by adjusting a single potential of ion mirror electrodes, preferably of the end electrodes.

56. The method of claim 38, wherein the said ion spatial and time-of-flight focusing by the said ion mirrors is achieved using mirrors with 4 to 7 electrodes while the spatial focusing transversely the plane of the folded ion path is achieved by incorporating a lens into the planar ion mirror, such lens having potential of opposite polarity relatively to the drift space.

57. The method of claim 38, wherein said ion mirrors are formed by fewer than 4 electrodes with a curved two-dimensional shape of electrodes.

58. The method of claim 38, wherein at least one electrode of at least one ion mirror is pulsed for ion gating in and/or out of the MR-TOF MS, or for initial acceleration, or for selection of number of cycles or for discarding of ions outside of the desired mass range.

59. The method of claim 38, wherein the set of periodic lens of the said MR-TOF MS is adjusted to make focal length F approximately equal to an integer number of quarter turns, F=N*P/4, where N=1,2,3...

60. The method of claim 38, wherein for the purpose of convenient tuning the periodic lens is substantially elongated across the shift axis.

61. The method of claim 38, wherein ions are reflected along the shift direction, using a constant and/or a pulsed operated reflection to form a folded path with or without repetitive segments, to gate ions in and out of the MR TOF MS, to bypass the MR TOF MS and to control number of repetition cycles.

62. The method of claim 38, wherein deflection plates are arranged within the drift space to provide mutual compensation of chromatic aberrations occurring in ion mirrors, lens and deflection plates.

63. A method of tandem mass spectrometric analysis (TOF MS-MS) comprising the sequential steps of parent ion formation and separation as in methods of claims 38 to 62; receiving parent ions, time separated according to their mass to charge ratio into a fragmentation cell; fragmenting at least some of parent ions in the fragmentation cell; mass analyzing at least a portion of productions.

64. The method of claim 63, wherein the product of the cell length L and gas pressure P in the cell is maintained above P*L> 0.2 Torr*cm, preferably P>0.5 Torr and L< 1cm, and wherein pumping is arranged differentially, being accompanied by electrostatic or a radio frequency ion focusing within intermediate pumping region.

65. The method of claim 63, wherein the step of ion fragmentation further comprises radial ion confinement by non-uniform radio frequency (RF) field and a step of controlling axial ion velocity by either an axial DC or an axial moving wave electric field.

66. The method of claim 63, wherein the said mass analysis of fragment ions comprises a step of time-of-flight separation in an additional time-of-flight mass spectrometer (TOF MS).

67. The method of claim 66, wherein the fragmentation time and flight time in the second TOF MS is at least 100 smaller compared to parent ions separation step in the first MR-TOF MS, and wherein data acquisition is suited for a 'parallel' analysis of non overlapping fragment spectra for multiple precursor ions.

68. The method of claim 66, wherein the said step of time-of-flight separation of fragment ions comprises multiple ion reflections in a multi reflecting spectrometer combined with a periodic focusing in the shift direction as in methods of claims 38 to 62.

69. The method of claim 68, comprising a step of adjusting of flight path in the second MR-TOF, preferably performed by reflecting ions in a shift direction.

70. The method of claim 63, for the purpose of versatility of tandem MS analysis further comprising switching between method 67 and method 68, said switching being preferably assisted by of acceleration voltage and of ion flight path in at least one time of flight analyzer.

71. The method of claim 63, wherein the step mass analyzing of product ions is performed in the same multi reflecting spectrometer and wherein ion flow is reverted either in the fragmentation cell or in the storage device of the pulsed ion source.

72. The method of claim 71, wherein further comprising steps of periodic storage and pulsed ejection of fragment ions out of fragmentation cell or out of storage device, said steps being preferably assisted by confining radio-frequency field and a time modulated axial DC field.

73. The method of claim 71, wherein flight path and flight time of fragment ions is much shorter compared to flight path and flight time of parent ions and wherein parallel MS-MS spectra are acquired similar to claim 67.

74. The method of claim 71, wherein flight times of parent and fragment separation are comparable and wherein a timed ion selection is performed prior to receiving ions into the fragmentation cell.

75. The method of claim 71, wherein steps of mass separation and fragmentation are repeated more than once to accomplish a so-called MSn analysis, preferably for structural studies or for determination of impurities.

76. The method of sample analysis comprising any of the above methods and a prior step of sample separation of the following list: liquid chromatography, electrophoresis, capillary electrophoresis, dialysis, affinity separation.

77. The method of sample analysis comprising any of the above methods and an additional step of mass separation in a mass spectrometer or mobility separation in a DC or field-asymmetric ion mobility spectrometer.

78. The method of sample analysis comprising any of the above methods and a step of gaseous ion reactions either in a gas filled ion storage compartments or in a fragmentation cell, said gaseous reactions including ion molecular reactions, ion-ion reactions, including ions of opposite polarities, ion electron reactions or illumination of ions by photons.